

The University of Chicago

THE CANNIZZARO REACTION OF
AROMATIC ALDEHYDES AS A
FUNCTION OF THEIR
PEROXIDE CONTENT

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE PHYSICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

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MABLE SCHAMP FOY

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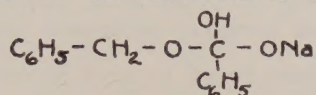


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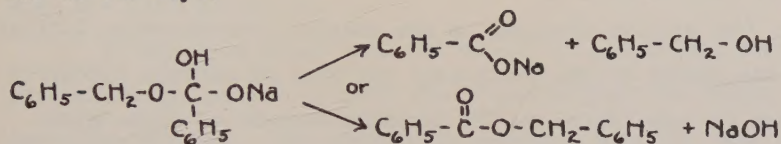
The author is very pleased to have had the privilege of working under the direction of Dr. M. S. Kharasch and is truly grateful for his painstaking supervision throughout this research.

INTRODUCTION

The disproportionation of benzaldehyde into benzoic acid and benzyl alcohol under the influence of alcoholic potash was first observed by Cannizzaro in 1853.¹ A mechanism for this reaction was proposed by Kohn and Tranton² on the basis of experiments on the action of sodium hydroxide on benzaldehyde in the absence of water, or in the presence of an excess of benzaldehyde. They had evidence of the formation of an ester-like intermediate:



This, in the presence of water, is hydrolyzed to benzyl alcohol and sodium benzoate; in the absence of water it may decompose in one of two ways:



The first reaction occurs more readily than the second and is favored by an excess of alkali. The second reaction is favored in the presence of an excess of aldehyde.

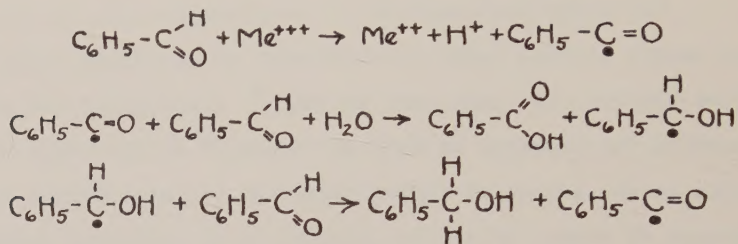
Haber and Willstätter³ believe that the Cannizzaro reaction differs from autoxidation only insofar as the function of free oxygen in that reaction is fulfilled by aldehyde molecules in the

¹Cannizzaro, Ann., **88**, 129 (1853).

²Kohn and Tranton, J. Chem. Soc., **75**, 1155 (1899); Proc., **15**, 194 (1899).

³Haber and Willstätter, Ber., **64B**, 2844-56 (1931).

Cannizzaro reaction. They claim that the Cannizzaro reaction is catalyzed by heavy metals, as is autoxidation. They give as a mechanism:



Benzaldehyde, which normally undergoes the Cannizzaro reaction readily, is sometimes found to give an anomalously low yield, and certain aldehydes are known not to undergo the Cannizzaro reaction at all. Radovsky has made an excellent review of this subject.⁴

The results obtained in the present investigation indicate that the extent of the Cannizzaro reaction of certain aldehydes depends to some degree on the peroxide content of these aldehydes. Three aromatic aldehydes were studied: benzaldehyde, p-toluidic aldehyde and anisaldehyde.

Anisaldehyde, which forms peroxides in the air most slowly of the three, allows of their most nearly complete removal, thus giving the most sharply defined results. Benzaldehyde, which is very strongly subject to autoxidation, is a difficult compound to work with, since peroxides cannot be completely and permanently removed. By comparing results of high and low peroxide content runs, it is apparent, however, that decrease in peroxide content

⁴Radovsky. "A Study of the Cannizzaro Reaction." Unpublished Master's Thesis, Department of Chemistry, University of Chicago, 1935.

of the aldehyde parallels decrease in the extent of Cannizzaro reaction.

Emulsifying agents slightly increase the rate of reaction. This is probably due to the presence of minute amounts of peroxide present in aldehyde assumed to be peroxide-free. The presence of small amounts of peroxide permits the reaction to take place to a small extent. The intimate mixing afforded by the presence of an emulsifying agent apparently increases the effectiveness of the peroxide present in its catalytic action.

Antioxidants, as is usual in peroxide-catalyzed reactions, cut down the yield significantly. Sodium hydrosulfite, a strong reducing agent, stable and active in alkaline solution, was found to be best. Catechol and hydroquinone probably are more effective, but decompose so rapidly in alkali in the presence of air that they are less practical.

It has been shown that the extent of Cannizzaro reaction when alcoholic potash is used also depends upon the amount of peroxides present. The Cannizzaro reaction does not take place when tertiary butyl alcohol is used as a solvent, if proper precautions are taken to exclude peroxides in carrying out the experiment.

EXPERIMENTAL

The technique for performing the Cannizzaro reaction in vacuo and in the absence of peroxides required the development of specialized apparatus and procedures. In outline the steps were as follows. The aldehyde to be used was purified and placed in a flask. By means of a ground joint in the neck of the flask it was attached to the vacuum line. Simultaneously, the alkali and water, or, in some cases the alkali, water and alcohol, were prepared for the reaction, placed in the reaction tubes, and sealed on the line. From three to eight reaction tubes were prepared and used in one vacuum experiment. The vacuum line was so arranged that the aldehyde could be distilled into the reaction tubes which already contained the alkali and solvent. Each tube contained about 10 cc. of 40-50% potassium hydroxide, when alcohol was not used, to which an approximately equal volume of the aldehyde was added. After the distillation of the aldehyde, in high vacuo, the reaction tubes were chilled and sealed under a high vacuum. During this time, one or more tubes were prepared using aldehyde that had not undergone the special purification process, in which the Cannizzaro reaction was to take place in the presence of air. The reactions taking place under these conditions were used as blanks by which to check the vacuum reactions. When the blanks and the vacuum reaction tubes were chilled and sealed, they were allowed to come to room temperature together, and placed on a shaker for a certain period of time. They were then opened and the contents rapidly washed out with large amounts of water and analyzed. In discussing the details

of this procedure it has been found advisable to divide it, somewhat arbitrarily, into several classifications.

The benzaldehyde, para-toluic aldehyde and anisaldehyde used in this work were Eastman products. When a new bottle of aldehyde was opened, its contents were redistilled and stored in a dark place until needed.

Chemically pure "Baker's Analyzed" potassium hydroxide pellets were used. They were kept in a dry airtight container, and all potassium hydroxide solutions were made up immediately before they were to be used. The antioxidants, acids and metal salts used in this work were from standard sources of supply. Every reagent used was tested for peroxide content before use. Peroxides used were made up freshly and stored in an icebox.

Preparation of peroxide-free aldehydes.--The weight of aldehyde that was to be used in a vacuum experiment was calculated. About one-half again as much aldehyde was measured out and washed in a separatory funnel with an excess of 3-5 molar sodium hydroxide solution. It was then washed twice with saturated sodium sulfite solution and finally with distilled water. It was important that these washing solutions have a greater density than the aldehyde used, except, of course, for the water. Before draining out the aldehyde, the stem of the funnel was washed out to prevent admixture of any impure aldehyde there with the purified material.

The washed aldehyde was then run into a previously prepared flask of but slightly greater volume, containing anhydrous sodium sulfate and a few crystals of catechol. The flask was stoppered tightly and shaken in an ice bath until the cloudiness had disappeared from the aldehyde. The material was then filtered quickly through glass wool into a flask with a ground neck,

containing 5-15 gms. of anhydrous sodium sulfite, which was to be placed on the vacuum line.

It was necessary in this purification to work quickly, allowing the aldehyde to be exposed to air as little as possible.

Preparation of the alkali.--When no alcohol was to be used, equal weights of C.P. potassium hydroxide pellets and distilled water were mixed and boiled carefully to remove dissolved air. The solution was allowed to cool without shaking to prevent redissolving of air. Approximately 10 cc. were poured into each reaction tube, in which had already been placed the desired amounts of antioxidant, if any was to be used. The reaction tubes were then sealed on the line.

When alcohol was used it was necessary to measure out and prepare the alcohol, water and potassium hydroxide separately for each reaction tube. Since two phases exist it was impossible otherwise to divide the material between several tubes with any certainty of identical proportions in all of them. Four gms. of alkali, 3 gms. of distilled water and 7 gms. of alcohol were used in each tube. For reactions involving ethyl alcohol or methyl alcohol as solvents, the alkali and water were weighed out and boiled as above, then poured into the tube and frozen with carbon dioxide snow-acetone mixture before the alcohol was added. The tube was again thoroughly chilled and sealed on the line, where it was evacuated before the mixture had become warm. These precautions were necessary in order to prevent atmospheric oxidation of the alcohol. If atmospheric oxidation did take place, as indicated by a yellow or brown color, the mixture was discarded. These precautions were not necessary in the case of tertiary butyl alcohol.

After the reaction tubes containing the potassium

hydroxide and solvent, and the flask containing the purified aldehyde, were in place on the vacuum line, a vacuum was established, and the contents of the tubes were heated thoroughly. When an alcohol was used, it was found advisable to heat the tubes under a vapor of the alcohol, to prevent excessive loss of the alcohol. At the same time the aldehyde was warmed gently to remove the remaining water and the air held by the crystals of sodium sulfite. In preparing extremely pure aldehyde, it was found desirable to perform one carefully fractionated distillation in the vacuum line, onto anhydrous sodium sulfite, before distilling the material into the reaction tubes.

The vacuum line.--The apparatus used for vacuum experiments is shown in Figure 1. The reaction tubes for vacuum work had a volume of from 25 to 50 cc. An effort was made to use tubes of approximately the same size for a single vacuum experiment. These tubes, between 2 and 3 cm. in diameter, had two openings, one in the top and one on the side. To each opening was sealed a slender tube; the side arm tube was bent upright 2 or 3 cm. from the reaction tube. The end of the side arm tube was constricted slightly and sealed to the vacuum line. This side arm connection did much to prevent bumping and splashing during the boiling-out procedure which, if uncontrolled, would have mixed the contents of the reaction vessels. The slender tube sealed to the top of the reaction tube was used for introducing the alkali solution, and also the alcohol and antioxidants, if these were to be used. In every case the antioxidants were added to the alkali solution before the reaction tube was closed or the aldehyde was distilled over. In some cases it was necessary to freeze the alkali solution to prevent admixture of the antioxidant with it. This in turn prevented decomposition of the

Note: "G.G." - ground glass joint

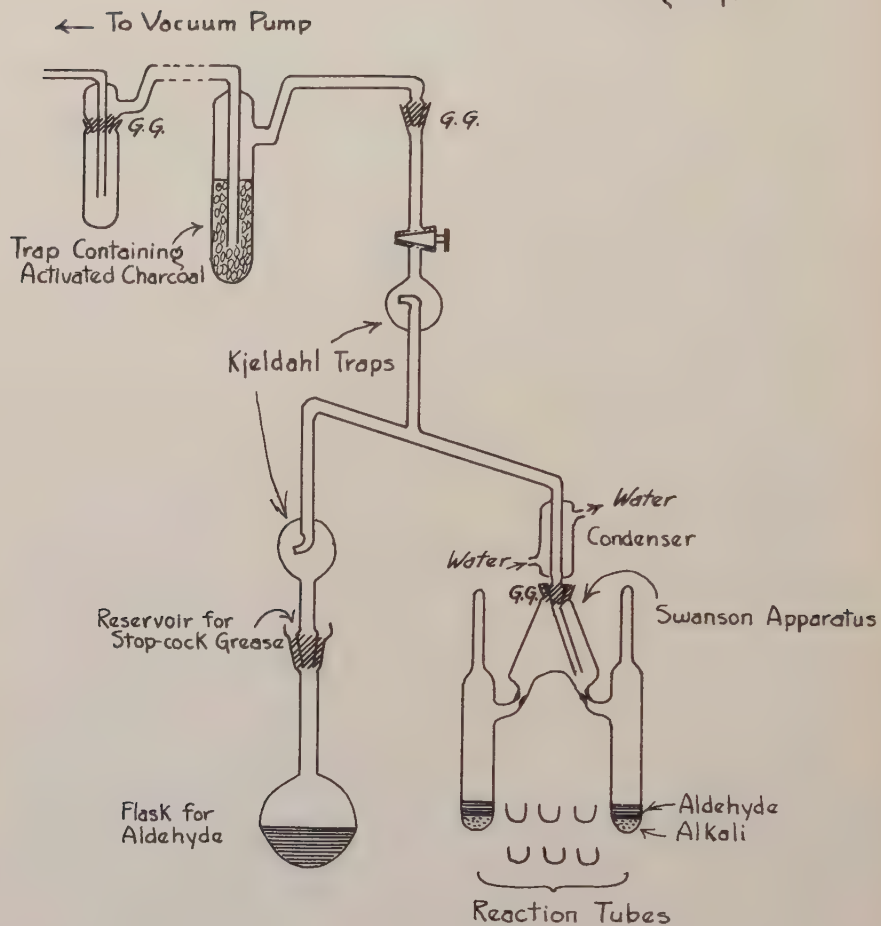


Fig. 1.--Apparatus for preparing reaction mixture for Cannizzaro reaction in vacuo.

antioxidant by the air in the presence of alkali. The vacuum line was so arranged that there were no stop cocks or other sources of lubricating grease between the aldehyde flask and the reaction tubes.

If alcohol was used it was found advisable, after chilling the mixture in the tube, to blow a gentle current of air through the tube for a moment to remove the alcohol vapors before sealing the tube to the line. Otherwise these vapors sometimes burned during the glassblowing. The upright arm was then sealed at the end, and the side arm was sealed on the vacuum line.

The flask for the aldehyde was connected to the line with a long ground-glass joint, fitted with a reservoir for stop-cock grease at the top, since the high temperatures attained sometimes, if prolonged, tended to melt the grease in the joint. A special high-melting grease was necessary in the case of the higher-boiling anisaldehyde.

The aldehyde was distilled across a yoke, through a short vertical condenser, and by means of a Swanson apparatus it was introduced into the reaction tubes. The first fraction was run into an empty tube and discarded. The yoke was connected to the main vacuum line through (1) a Kjeldahl trap, (2) a stopcock, (3) a ground glass joint, and (4) a trap containing activated charcoal. While water and alcohol vapors were being passed into the line the charcoal trap was not used, but the vapors were caught in a trap equipped with a ground glass joint so that it could be emptied between runs.

Numerous ground joints permitted this type of line to be taken down and cleansed between runs, an essential factor in the use of a high-boiling liquid in a vacuum line.

Distillation of the aldehyde into the reaction tube.--If

pinholes were found after the vacuum was established, they were mended and the vacuum re-established very quickly. After all the liquids were thoroughly boiled out and re-cooled, a vacuum of 10^{-3} to 10^{-5} millimeters of mercury was obtained and, with the yoke open to the vacuum, distillation of the aldehyde into the first, or discard, tube was begun. A stop-cock between the yolk and the vacuum pump was closed just before distillation into the reaction tubes was begun. An amount of aldehyde about equal in volume to the alkali solution in the tubes was distilled into each tube. After each reaction tube contained the proper amount, the aldehyde flask was allowed to cool, and the stop-cock was again opened, in order to displace any traces of air with aldehyde vapor and to remove aldehyde from the surfaces to be sealed off.

The tubes were then sealed off separately, and the stop-cock closed to prevent an excessive amount of aldehyde from passing over to the trap.

The runs made in air were prepared in plain tubes, without the side arm. The obvious precautions were taken to insure that concentration of alkali, etc., would be paralleled as nearly as possible between these tubes and the vacuum runs.

All the tubes were then placed in a shaker. When comparisons between different sets of reactions were to be made, a rotating shaker in a thermostat at 25°C. was used. Otherwise a cradle shaker at room temperature was used.

The analysis.--After the desired period of time the tubes were opened by breaking off the end of the upright tube.

Analysis of their contents was effected by dilution with water, a series of extractions with ether, acidification, and a second series of extractions with ether. The ether was boiled off gently on a steam bath and the two residues were weighed.

Benzaldehyde and benzyl alcohol were assumed to be the only compounds in the first residue and benzoic acid in the second.

Experiments were made to determine the accuracy of the analytical method. Weighed amounts of benzaldehyde, benzyl alcohol and benzoic acid were shaken with 12.5% potassium hydroxide solution and the mixture handled exactly as though it were the contents of a reaction tube after dilution. The degree of variation found by these experiments between the amounts of materials used and that found, was never greater than 10%, and usually less than 5%. These results indicate that the percentages given in the tables for the extent of reaction are accurate within $\pm 5\%$.

The peroxide test.--The peroxide content of the various materials used was measured in air by the standard micro method, using one crystal of ferrous ammonium sulfate, 5 cc. of 10% ammonium thiocyanate solution and a drop of the material to be tested. A red color indicated a positive peroxide content. In every peroxide test a blank was made for purposes of comparison. The strength of these peroxide tests was designated by the notations: "negative," "1+," "2+," "3+," "4+."

Peroxide tests made in vacuo involved the same reaction, but the technique of performing them was more complex. (See Figure 2.) A few crystals of ferrous ammonium sulfate were placed in each of the two small inner tubes, and 5 cc. of 10% ammonium thiocyanate solution were placed in each of the two larger, outer tubes. The tubes were frozen slowly and sealed to the vacuum line, where, after evacuation, a few drops of the material to be tested were distilled into the vertical tube. Both tubes were then sealed off at their individual constrictions, brought to room temperature, and shaken thoroughly. The one without any of the material to be tested was the blank against

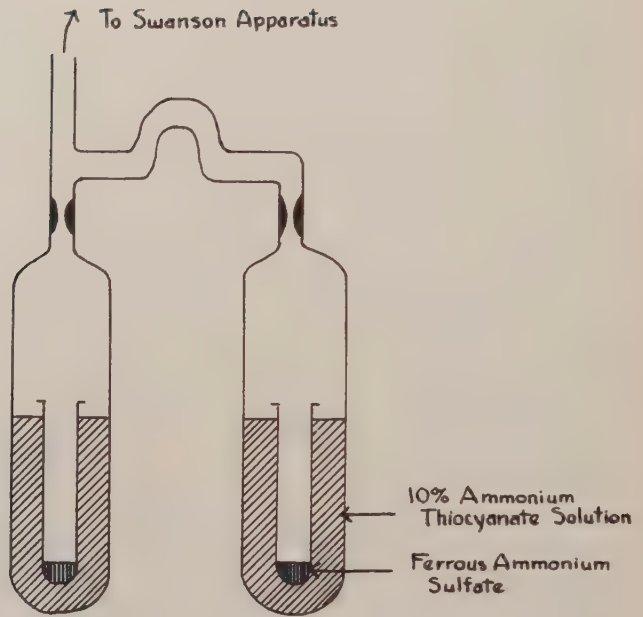


Fig. 2.--Apparatus for peroxide test in vacuo.

which the other was checked. A negative test required that the intensity of the red color in the two tubes be identical. The designation of the degree of peroxide content in the cases where the two colors were not identical, in the terms mentioned above, cannot be exactly described, since it depends upon the investigator, and upon the experience of having made a large number of such tests.

If the peroxide test in vacuo was greater than 1+ on benzaldehyde that was to have been used in preparing vacuum tubes, the material was discarded. In the cases of anisaldehyde and para-toluic aldehyde, the peroxide test in vacuo on the purified material was required to be negative before the material was used. The peroxide contents of the aldehydes used for blanks were measured in air and in the tabulated results are designated by the above scale.

DISCUSSION OF RESULTS

In general, the experiments discussed here were carried out in groups; each group of reactions was designed to clarify one aspect of the problem. Usually, from three to five vacuum reactions were carried out simultaneously with one or more "blanks." Thus, as nearly identical experimental conditions as possible applied for all the reactions performed at one time. The antioxidant, emulsifying agent or catalyst added to the reaction mixture varied for different reaction tubes.

With para-toluic aldehyde a series of experiments was made in order to investigate, first, the differences between the yields of reactions carried out under peroxide-free conditions and those carried out in the ordinary manner. Then the effect of a metallic catalyst, ferric chloride, was investigated. Finally, the effect of an emulsifying agent, toluic acid, was studied. The results of these investigations are given in Table I.

Explanation of the tables.--Each of the experiments for which data are given in the tables has been checked at least one time unless otherwise stated. Since a single experiment is valuable only insofar as it can be compared with another experiment under altered conditions, checks were considered satisfactory if the relations between the results of a group of experiments were duplicated, rather than if the exact percentages denoting the extent of the reaction were repeated. No attempt was made to adjust factors such as the age of the aldehyde, the exact concentration of the alkali solution, and variations of a few degrees in temperature between two identical sets of

reactions, because these factors are not important in obtaining checks for relationships between reaction rates.

Some data which were obtained early in the experimental work, before the technique of the vacuum experiments was fully developed, could not be checked. Since all experiments were repeated until it could be accurately checked, the omission of such faulty data is considered fully justified.

The term "vacuum reaction" as used in the tables indicates that the reaction took place in a tube prepared on the vacuum line as has been described. The column marked "peroxide content" lists the peroxide content of the aldehyde used in the various reactions. This was measured, in the case of vacuum reactions, by the vacuum method described above, immediately before the aldehyde was distilled into the reaction tubes. It was measured for the blanks either just before or just after the materials were mixed. These experiments were performed in groups, precisely the same experimental conditions applying to the reactions within one bracket.

From a study of Tables I and II it can be observed that para-toluic aldehyde and anisaldehyde react similarly. Reactions 1 and 2 in both tables show that peroxide-free aldehyde, reacting under conditions eliminating the possibility of peroxide formation, does not undergo the Cannizzaro reaction appreciably in the periods stated. The blanks, run under precisely identical conditions except that peroxides and air are not removed, react appreciably (33% for toluic aldehyde and 25% for anisaldehyde.) Reactions I-3, I-4 and I-5, performed simultaneously, show that with para-toluic aldehyde the peroxides present in the aldehyde (reaction 5) are much more effective catalysts for the reaction than is FeCl_3 (reaction 4).

We find in Table I, reactions 6 and 7, and in Table II, reactions 3, 4, 5 and 6, that the catalytic action of FeCl_3 is much more pronounced when oxygen is introduced over the reaction

TABLE I
THE PEROXIDE EFFECT IN THE CANNIZZARO REACTION
WITH PARA-TOLUIC ALDEHYDE

Conditions Applying to Reactions	Peroxide Content	Time in Hours	Extent of Cannizzaro Reaction (Per Cent)
{ 1 Vacuum reaction	neg.	8	0
{ 2 Blank	3+	8	33
{ 3 Vacuum reaction	neg.	22	2
{ 4 Vacuum reaction; 0.1 gms. FeCl_3 added	neg.	22	12
{ 5 Blank	3+	22	91
{ 6 Vacuum reaction; 0.2 gms. FeCl_3 added	neg.	20	8
{ 7 Vacuum reaction; 0.5 gms. toluic acid added	neg.	20	0
{ 8 Vacuum reaction; O_2 used;* 0.2 gms. FeCl_3 added	neg.	20	38
{ 9 Blank	4+	20	100

*In some reactions it was found desirable to supply an atmosphere of oxygen over a reaction mixture which had been prepared on the vacuum line. In such cases, after the reaction tube was sealed off the line, the end of the slender upright tube was broken off while the contents were still frozen, and oxygen was passed in through a very fine glass tube for exactly three minutes. The tube was then re-sealed.

mixture. Even under these conditions, however, the reaction does not proceed as far as when the anisaldehyde is not treated for removal of peroxides. From I-7, II-7 and II-8 it is seen that the presence of the acid corresponding to the aldehyde used does not increase the extent of the reaction; thus the treatment of

the aldehyde, which removes acid as well as peroxides, does not render the yield low because of the absence of acid as an impurity in the aldehyde.

TABLE II
THE PEROXIDE EFFECT IN THE CANNIZZARO REACTION
WITH ANISALDEHYDE

Conditions Applying to Reactions	Peroxide Content	Time in Hours	Extent of Cannizzaro Reaction (Per Cent)
{ 1 Vacuum reaction	neg.	(30 days)	0
{ 2 Blank	3+	12	25
{ 3 Vacuum reaction	neg.	8	0
{ 4 Vacuum reaction; 0.1 gms. FeCl ₃ added	neg.	8	1
{ 5 Vacuum reaction; O ₂ used;* 0.1 gms. FeCl ₃ added	neg.	8	14
{ 6 Blank	3+	8	35
{ 7 Vacuum reaction	neg.	20	0
{ 8 Vacuum reaction; 0.5 gms. anisic acid added	neg.	20	0
{ 9 Vacuum reaction; O ₂ used*	neg.	20	7
{ 10 Blank	3+	20	30
{ 11 Vacuum reaction	neg.	20	1
{ 12 Vacuum reaction; 0.1 gms. FeCl ₃ added	neg.	20	3
{ 13 Vacuum reaction; O ₂ used;* 0.1 gms. FeCl ₃ added	neg.	20	42
{ 14 Blank	3+	20	84

*See footnote, Table I.

In each group of reactions a blank was prepared for the sake of general comparison.

Benzaldehyde presented more difficulties than the two aldehydes discussed above. Of the three aromatic aldehydes

studied, benzaldehyde shows itself to be the most sensitive to autoxidation. While it was not difficult to purify anisaldehyde and para-toluic aldehyde to such an extent that a peroxide test in vacuo was negative, it frequently occurred that the most careful purification of benzaldehyde left a small amount of peroxides (1+) present at the time the test was made in vacuo. In addition to this, benzaldehyde undergoes the Cannizzaro reaction more rapidly under ordinary conditions than the other aldehydes studied. Thus partial removal of peroxides was frequently insufficient to show appreciable deviation from the normal reaction.

The technique of carrying out Cannizzaro reactions under peroxide- and oxygen-free conditions was developed with benzaldehyde. The data for benzaldehyde therefore show the wide variations contingent on the development of a new method of handling a reaction. For these reasons, not all of the reactions undergone by benzaldehyde are comparable with one another. Reactions prepared and carried out in a single vacuum experiment, with the blanks corresponding, are in each case enclosed in a bracket in the tables. Only the results of the reactions within a bracket are comparable with one another, except when exactly the same conditions apply to reactions in two different brackets, and the yields of the two similar reactions are the same. In these cases, the results in two different brackets can be compared.

The work done with benzaldehyde was more exhaustive than with para-toluic aldehyde or anisaldehyde. A study of the effect of antioxidants on the extent of reaction was first taken up (Table III). The effect of added peroxides on the extent of the Cannizzaro reaction was studied (Table IV). The problem of emulsifying action, both of the peroxides added and of benzoic

TABLE III

THE EFFECT OF ANTIOXIDANTS ON THE CANNIZZARO
REACTION WITH BENZALDEHYDE

Conditions Applying to Reactions	Peroxide Content	Time in Hours	Gms. Anti- oxidant added	Extent of Cannizzaro Reaction (Per Cent)
A. Sodium Sulfite				
1 Vacuum reaction	..	2	0.1	7
2 Air reaction; benz- aldehyde washed with dilute NaOH and dried	4+	2	...	12
3 Blank - untreated	4+	2	...	30
4 Vacuum reaction	..	3	0.1	20
5 Air reaction; washed with di- lute NaOH and dried	4+	3	...	40
6 Blank	4+	3	...	50
B. Sodium hydrosulfite*				
7 Air reaction	2+	4 $\frac{1}{8}$	0.1	16
8 Air reaction	2+	4 $\frac{1}{8}$	0.5 benzoyl peroxide	90
9 Blank	2+	4 $\frac{1}{8}$	...	29
10 Vacuum reaction	..	4	0.2 1/50,000 cupric ion	3
11 Vacuum reaction	..	4	...	15
12 Vacuum reaction	..	4	0.2	5
13 Vacuum reaction	..	4	...	15
C. Catechol				
14 Vacuum reaction	..	4	0.2 Na ₂ S ₂ O ₄	7
15 Vacuum reaction	..	4	...	16
16 Vacuum reaction	..	4	0.5	1
17 Air reaction	3+	4	0.5	15
18 Blank	3+	4	...	35

TABLE III--CONTINUED

Conditions Applying to Reactions	Peroxide Content	Time in Hours	Gms. Anti-oxidant Added	Extent of Cannizzaro Reaction (Per Cent)
D. Hydroquinone				
19 Vacuum reaction		4	0.2 Na ₂ S ₂ O ₄	4
20 Vacuum reaction		4	0.5	5
21 Air reaction	3+	4	0.5	30
22 Blank	3+	4	...	30

*All runs checked at least three times.

acid removed by purification of the benzaldehyde was studied carefully through experiments involving the controlled addition of benzoic acid or sodium benzoate to the reaction mixture. Data on these experiments appear in Table V. In an attempt to emphasize the difference between the reaction rates of ordinary benzaldehyde, reacting in the presence of air, and benzaldehyde treated in a way to remove peroxides, reacting in the absence of oxygen, data for reaction rate curves were obtained. These data appear in Table VI. The effect of the presence of various alcohols on the reaction was then investigated. These data are in Tables VII, VIII and IX.

The Effect of Antioxidants.--Different antioxidants were examined as to their efficacy in slowing down the rate of the Cannizzaro reaction with benzaldehyde. The results of these experiments are shown in Table III. Reactions designated as "air" in this table were those in which the reactants were prepared, mixed and shaken in the presence of air, as differentiated from "vacuum reactions." In all of these reactions approximately

10 cc. of 40-50% potassium hydroxide solution and 10 cc. of benzaldehyde were used.

It is apparent from these data that sodium hydrosulfite, catechol and hydroquinone are good negative catalysts for the Cannizzaro reaction. The first is particularly efficacious when used in conjunction with one part in fifty thousand by weight of cupric ion. This amount of cupric ion was supplied by the use of a measured amount of a quantitative solution of cupric sulfate, in place of an equal amount of water, in making up the solution of potassium hydroxide. Catechol and hydroquinone decompose rapidly in an alkaline medium when exposed to air or oxygen. Because of this it is difficult to obtain reproducible results when these materials are used as antioxidants. On the other hand, sodium hydrosulfite is stable in air in an alkaline medium and is as efficacious an antioxidant as either of the others when they act under optimum conditions.

Through comparing reactions 2 and 3 in Table III, and also reactions 5 and 6, it is observed that even in the presence of air removal of excess peroxides by washing the benzaldehyde with dilute sodium hydroxide decreases the yield in the Cannizzaro reaction appreciably. However, the use of an antioxidant in a vacuum reaction decreases the yield to a much greater extent. In reactions 7, 8 and 9 it appears that, while sodium hydrosulfite decreases the yield of a reaction carried out under ordinary conditions, benzoyl peroxide greatly increases it. Reactions 10 and 11 in this table show the effectiveness of sodium hydrosulfite in combination with one part in fifty thousand of cupric ion in slowing the Cannizzaro reaction. Tables IIIC and IIID list reactions devised to compare the effectiveness of sodium hydrosulfite with catechol and hydroquinone respectively.

The effect of peroxides.--A series of reactions was carried out in order to examine the effects of addition of known amounts of peroxides to samples of benzaldehyde which had been treated to remove peroxides.

TABLE IV
THE EFFECT OF ADDED PEROXIDES ON THE CANNIZZARO
REACTION WITH BENZALDEHYDE

Conditions Applying to Reactions	Time in Hours	Antioxidants or Peroxide Added	Extent of Cannizzaro Reaction (Per Cent)
A. Benzoyl Peroxide			
{ 1 Air	4	0.5	90
{ 2 Blank	4	...	29
{ 3 Air; benzaldehyde washed with NaOH, H ₂ O	4	...	35
{ 4 Air; benzaldehyde washed with NaOH, H ₂ O	4	0.2 gm. Na ₂ S ₂ O ₄ / 1/50,000 cu- pric ion	20
{ 5 Nitrogen; benzaldehyde washed with NaOH, H ₂ O	4	...	10
{ 6 Air; benzaldehyde washed with NaOH, H ₂ O	4	0.5	40
B. Oxygen			
{ 7 Vacuum reaction	4	...	20
{ 8 Oxygen	4	...	44
{ 9 Blank	4	...	32

It was also found that it was possible to use too little of the antioxidant, although, as would be expected, an excess had no effect. Experiments were run in vacuo in an attempt to find the minimum of hydrosulfite necessary. One part in 50,000

by weight of cupric ion was added to catalyze the action of the antioxidant in each of the following cases:

Per Cent Sodium Hydrosulfite	Extent Cannizzaro in Four Hours
9.0	0.5
1.5	1.4
0.6	2.0

When only that amount of sodium hydrosulfite soluble in the 50% potassium hydroxide solution was used, the extent of Cannizzaro reaction after four hours of shaking was 9%.

From the results of Table IV it can be seen that in general the addition of peroxides increases the rate of the Cannizzaro reaction. Reactions 1 and 2 are a comparison of the extent of two Cannizzaro reactions carried out in the presence of air, with and without one-half gram of benzoyl peroxide. It is evident that this addition results in tripling the extent of the reaction in four hours. Reactions 3, 4, 5 and 6 show, again using reactions taking place under ordinary conditions, the effect of the air above the reaction mixture, since the use of an atmosphere of nitrogen cuts the yield to one-third of that with an atmosphere of air. Also, the effect of adding anti-oxidant (reaction 4) or peroxide (reaction 6) can be seen in this series of reactions. The effect of the use of an atmosphere of oxygen over the reaction mixture is shown by Table IV B, which indicates that the reaction is accelerated by the presence of peroxideogenic materials.

The effect of emulsifying agents.--Further experiments were performed in order to show the difference between the action of the peroxides as such and simply as emulsifying agents. These data are to be found in Table V.

The results in Table V show that the action of perbenzoic

TABLE V

THE EFFECT OF EMULSIFYING AGENTS ON THE CANNIZZARO REACTION WITH BENZALDEHYDE

Conditions Applying to Reactions	Time in Hours	Agents Added	Extent of Cannizzaro Reaction (Per Cent)
A. Benzoyl peroxide			
1 Vacuum reaction	4	1/50,000 cupric ion, 0.5 gms. $\text{Na}_2\text{S}_2\text{O}_4$ and 0.2 gms. benzoic acid	10
2 Vacuum reaction	4	1/50,000 cupric ion and 0.5 gms. $\text{Na}_2\text{S}_2\text{O}_4$	1
3 Vacuum technique, air admitted	4	0.5 gms. benzoyl peroxide	88
4 Blank	4		42
B. Perbenzoic acid			
5 Vacuum reaction	4	...	12
6 Vacuum reaction	4	0.5 gms. perbenzoic acid	25
7 Vacuum reaction	4	0.6 gms. sodium benzoate	15
8 Vacuum reaction	4	...	4
9 Vacuum reaction	4	0.5 gms. perbenzoic acid	40
10 Vacuum reaction	4	0.6 gms. sodium benzoate	6
C. Benzoic acid			
11 Vacuum reaction	4	...	12
12 Vacuum reaction	4	0.5 gms. benzoic acid	15
13 Vacuum reaction	4	0.5 gms. benzoic acid, 0.5 gms. $\text{Na}_2\text{S}_2\text{O}_4$	7

acid and benzoyl peroxide in accelerating the Cannizzaro reaction are not due only to their emulsifying action, since the use of benzoic acid and sodium benzoate in approximately equivalent amounts does not result in such large increases in the extent of reaction in the periods given. Table V A gives a comparison

between a vacuum reaction with antioxidant, a similar reaction mixture containing benzoic acid, and a third reaction without the antioxidant, but with benzoyl peroxide. This third reaction tube was prepared exactly like the other two, but opened to the air for a moment before sealing it off. It is seen that the emulsifying agent increases the yield 87%. Table V B shows the same thing in the case of perbenzoic acid and sodium benzoate. Table V C shows that the effect of benzoic acid in increasing the yield even by a small percentage is not due to any real catalytic action of the benzoic acid, but simply to its action in increasing the intimacy of mixing the two phases involved in the reaction.

Data for rate curves.--Reactions were run over various periods of time in order to show the effects of careful purification of benzaldehyde and of carrying out the reaction so that oxygen is excluded. These data are shown in Table VI. Table VI B and C show the difference between the rate of the reaction with an old sample of benzaldehyde (B) and with a sample from a freshly opened bottle (C).

Inspection of these data and the corresponding graphs shows that a straight line curve results in the range covered by the experiments when the peroxide content of the reaction mixture is high. As the peroxide content is decreased (curve C), the rate of reaction increases as the extent of the reaction increases. This may be due, to a large extent, to the formation, through the reaction, of potassium benzoate which acts as an emulsifying agent.

The effect of solvents.--Ethyl alcohol was first used as a solvent in the reaction, and in spite of the greatest precautions in removing peroxides and oxygen, it was impossible

TABLE VI

DATA FOR RATE CURVES OF THE CANNIZZARO
REACTION UNDER VARIOUS CONDITIONS*

Conditions Applying to Reactions	Time in Hours	Extent of Cannizzaro Reaction (Per Cent)	
		Series 1	Series 2
A. Vacuum reactions	4	1.0	2.8
	6	6.0	5.7
	8	12.0	10.0
B. Air reactions with untreated aldehyde; perox- ide test 4 ⁺	4	43.0	48.0
	6	64.0	63.0
	8	80.0	98.0
C. Air reactions with untreated aldehyde; perox- ide test 3 ⁺	4	12.0	
	6	27.0	
	8	53.0	
D. Air reactions with aldehyde which had been shaken with anhy- drous Na ₂ SO ₃ and 1 gm. Na ₂ S ₂ O ₄ added	4	8.0	
	6	12.0	
	8	17.0	

*See Figure 3.

to reduce the extent of the reaction appreciably. Four grams of potassium hydroxide, 3 gms. of distilled water, and 7 gms. of absolute ethyl alcohol were used with about 10 gms. of aldehyde.

The use of antioxidants in these reactions did not decrease the yields appreciably.

These results led us to investigate the possibilities of using other solvents in the reaction, not only to cut down the rate, but also to discover the reason for the apparent abnormalities when ethyl alcohol is used as a solvent. Methyl alcohol and tertiary butyl alcohol were tried as solvents, with ethyl

RATE OF CANNIZZARO REACTION - BENZALDEHYDE

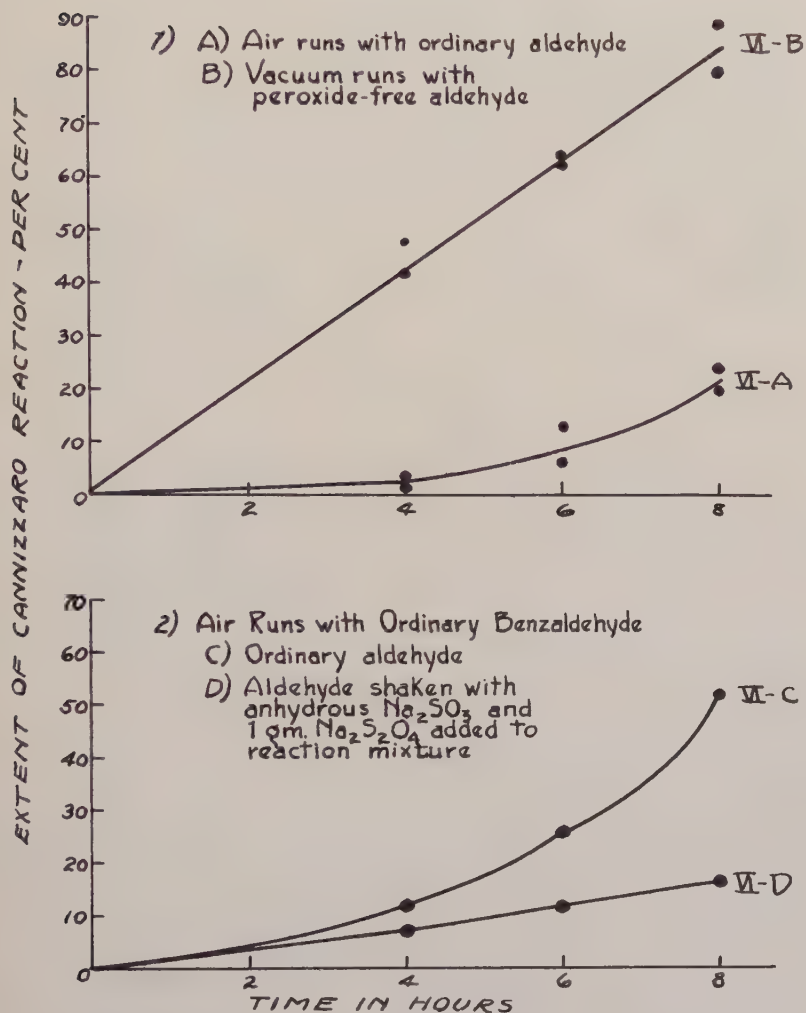


Fig. 3.

TABLE VII

THE USE OF ETHYL ALCOHOL AS A SOLVENT
FOR THE CANNIZZARO REACTION

Conditions Applying to Reactions	Time in Hours	Extent of Cannizzaro Reaction (Per Cent)
Para-toluic aldehyde		
Vacuum reaction	12	80
Vacuum reaction, with O ₂ passed through for 3 minutes	12	89
Blank	12	100
Anisaldehyde		
Vacuum reaction	4	20
Blank	4	60
Vacuum reaction	12	92
Blank	12	100

TABLE VIII

THE EFFECT OF SOLVENTS ON THE CANNIZZARO
REACTION (IN VACUO) WITH ANISALDEHYDE

Solvent	Time in Hours	Extent of Cannizzaro Reaction (Per Cent)
Methyl alcohol	3	5
Ethyl alcohol	3	42
Tertiary butyl alcohol	3	0
Tertiary butyl alcohol*	3	6

*Air reactions with untreated anisaldehyde.

alcohol for comparison. The results are in Table VIII.

Reactions were carried out with different time periods with anisaldehyde and benzaldehyde, with tertiary butyl alcohol as a solvent. Table IX shows the results.

TABLE IX
THE USE OF t-BUTYL ALCOHOL AS A SOLVENT
FOR THE CANNIZZARO REACTION

Conditions Applying to Reactions	Time in Hours	Extent of Cannizzaro Reaction (Per Cent)
Anisaldehyde		
Vacuum reaction	4	0
Vacuum reaction; O ₂ passed through for exactly 3 minutes	4	10
Vacuum reaction; O ₂ passed through for 3 minutes	8	16
Vacuum reaction	8	5.5
Benzaldehyde		
Vacuum reaction	3	17
Vacuum reaction	5	29
Vacuum reaction; O ₂ passed through for 3 minutes	3	52
Vacuum reaction; O ₂ passed through for 3 minutes	3	78

From Tables VIII and IX it is seen that in the presence of tertiary butyl alcohol aldehydes undergo the Cannizzaro reaction in a manner consistent with the other results outlined here. The effect of ethyl alcohol, and to a lesser extent, methyl alcohol, in catalyzing the reaction cannot be explained.

Summary.--Tables I and II show the effect on the extent of the Cannizzaro reaction of removing peroxides and peroxidogenic materials from the reaction mixtures in the cases of para-toluic aldehyde and anisaldehyde. It is shown there that

the absence of the acid corresponding to the aldehyde is not the important factor in decreasing the yield in the Cannizzaro reaction, nor is the presence of salts of a heavy metal such as iron a catalyst for the reaction. In a more detailed study of the relationship between peroxide content of the aldehyde and extent of the Cannizzaro reaction, benzaldehyde was used. Table III outlines the experiments which show that antioxidants retard the reaction. Sodium hydrosulfite used in conjunction with one part in 50,000 of cupric ion was found to be the most effective antioxidant. In Table IV, the effect of adding peroxides to the purified reaction mixture is studied. The peroxides used were perbenzoic acid and benzoyl peroxide. It was found that in every case the presence of this type of compound increases the yield in the Cannizzaro reaction enormously over the yield in the absence of these compounds. The effect of oxygen and of air over the reaction mixture was also studied, and it was shown that an atmosphere of nitrogen causes a decrease in the yield, an atmosphere of oxygen causes an increase, in comparison with the yield when the reaction takes place under air. Table V contains the results of a series of reactions made in an effort to determine whether the action of benzoyl peroxide and perbenzoic acid was due to their emulsifying effects or was the result of their being peroxides. In this series of studies on benzaldehyde, an attempt was made to show that peroxides, and nothing other than peroxides, cause the deviation in yield noticed between Cannizzaro reactions made under vacuum conditions with specially purified reagents and Cannizzaro reactions performed in an atmosphere of air, with reagents that have not been specially treated.

Finally, a series of reactions was arranged with varying time periods, so that the effect of removal or partial removal

of peroxides on the entire rate curve of the reaction could be gauged. It was found that the slope of the rate curve increases with time. It is indicated that this increase is not directly a function of time, but rather a function of the extent of reaction over a period of time, since this rise appears much earlier in cases where the reaction is fast than when it is slow.

CONCLUSIONS

1. It has been shown that the rate of the Cannizzaro reaction in cases of benzaldehyde, para-toluic aldehyde and anisaldehyde depends upon the amount of peroxide present, as well as the temperature, concentration of the potassium hydroxide solution used, the presence of solvents or emulsifying agents, and other factors.

2. The amount of the corresponding acid present has an appreciable effect on the rate of the reaction, but it is not identical with that of peroxides.

3. As the peroxide content of the aldehyde is decreased, the rate of the reaction approaches zero.

4. Antioxidants which are effective in alkaline medium decrease the extent of Cannizzaro reaction.

5. The use as a solvent of an alcohol in the Cannizzaro reaction increases the extent of reaction in the cases of ethyl alcohol and methyl alcohol. When tertiary butyl alcohol is used, and peroxides have been removed, the extent of the Cannizzaro reaction is greatly decreased.

6. A vacuum line and technique for the handling of high-boiling, easily oxidized liquids in vacuo has been devised and described.

